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EXAMINER	
RILEY, JEZIA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,007	MIRKIN ET AL.	
	Examiner	Art Unit	
	Jezia Riley	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *433-437 and 439-446* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *433-437 and 439-446* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

1. Applicants' arguments and amendments, filed on3/23/04, have been approved and entered. They have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Non-Statutory Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 433-437, 439-446 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 237-265 of copending Application No. 09/975,376.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both application are claiming nanoparticles comprising oligonucleotides attached thereto, at a density sufficient so that the nanoparticles are stable.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 433-437, 439-446 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433, 446 and 461-474 of copending Application No. 09/975,059. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compositions of 09/975,059 comprises species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 433-437, 439-446 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kossovsky et al. (USPN 5,460,831).

Kossovsky et al. discloses DNA or RNA attached to a nanocrystalline core particle and coated with a targeting ligand or membrane to provide a viral transfection system which may be used in gene therapy. The invention is based in part on the discovery that the surface of ultrafine particles (nanocrystalline particles) can be modified with a surface coating to allow attachment of transfecting DNA or RNA to

produce compositions wherein the naturally occurring structural environment of the DNA or RNA is mimicked sufficiently so that biological activity is preserved. The core particle, with the surface coating and attached transfecting DNA or RNA, is further coated with a targeting agent, such as ligand or phospholipid membrane complex to provide targeting of the DNA or RNA to particular cell receptors.

The DNA/RNAparticle construct is targeted to a specific tissue or cell type. In order to achieve this targeting, the construct has a targeting ligand or a primed phospholipid membrane tightly adsorbed to its surface. The membrane may contain proteins, receptors and carbohydrates which provide targeting of the vehicle. The membrane also serves to further maintain the stability of the transfecting DNA or RNA and the integrity of the construct.

The core particles may be made from a variety of inorganic materials including metals or ceramics. Preferred metals and alloys include beryllium, silicon, gallium, copper, gold, titanium, nickel, aluminum, silver, iron, steels, cobalt-chrome alloys, and titanium alloys. Therefore Kossovsky teaches the attachment of an oligonucleotide to a gold nanoparticle at a surface density sufficient so that the nanoparticles are stable (see abstract, cols. 3-4 and Examples 1-13).

8. Claims 433-437, 439-446 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kausch et al. (USPN 5,665,582).

Kausch et al. discloses a method for the isolation and sorting of biological materials. Biological material includes chromosomes, segments of chromosomes, cell organelles, or other minute cellular components. The biological material is separated from the cellular milieu, if necessary, and anchored to a support. Examples of a support are glass coverslips, glass or polymer beads. The anchoring is by means of a reversible polymer and cross-linking system. The supported biological material may then be labelled with compositions capable of binding to said material, and with magnetic particles. Examples of the binding material include nucleic acid probes and antibodies. An example of the antibodies would be those directed to histones. Other labels, for example, fluorescein-biotin-avidin may be used. The material may be released from the support and sorted by a magnetic force. This method is an alternative to flow cytometry and presents numerous advantages in terms of time, resolution, purity, and preservation of the structure of the biological material during isolation and separation.

The binding composition may further comprise an indicator such as a luminescent indicator, a radioactive indicator, or an electron opaque indicator, such as i.e. colloidal gold, with a preferred indicator being a fluorescent indicator, so that the binding can be detected by some means. Preferred means of detecting include, but are not limited to fluorescence, autoradiography and electron microscopy. Therefore Kausch teaches the attachment of an oligonucleotide to a gold nanoparticle at a surface density sufficient so that the nanoparticles are stable (see abstract, cols. 4-10, 17-19, 24 and Examples 1, 2 and 4-8).

9. Claims 433-437, 439-446 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yguerabide et al. (6,214,560).

Yguerabide et al. discloses a method of light illumination and detection named "DLASLPD" (direct light angled for scattered light only from particle detected), which is an analyte assay using gold particulate label for specific detection of one or more analytes in a sample. One or more analytes in a sample can be detected and measured by detection and/or measurement of one or more of the specific light scattering properties of metal-like particles. (Summary of the Invention). For example, a certain nucleic acid analyte is composed of about 100 nucleic acid bases and is present in a sample. The sample is prepared so that this nucleic acid is in a single stranded form. Then two or more unique single-stranded "probe" nucleic acid sequences are added to the sample where these different probes bind to different regions of the target strand. Each of these probes has attached to one or more particles (col. 74). Further, the particles can form different types of aggregates that can be detected visually or instrumentally in a microscope or through macroscopic observation or measurements without having to separate free from analyte bound particles. Low particle surface density (less than 0.1 particles per mu^2) on a spot and high particle surface density (greater than 0.1 particles per mu^2) on a spot are also disclosed which are viewed to be inclusive of the instant claims.

In certain analytical and diagnostic assays, it may be preferable to increase the detectability of the scattered light properties of the particles so that very simplified or no

detection instrumentation is required. By use of the appropriate molecular recognition binding-pairs and particles it is possible to significantly increase the level of detection sensitivity. Single-stranded homopolymer sequences, avidin-biotin, streptavidin-biotin, and other binding-pair systems can be used to "chain-together" and "build-up" many particles (col. 73-76).

The reference describes methods of attachment of substances to particles and other surfaces. In this method of attaching substances to particles or other surfaces, a two step approach which involves the use of base material molecules is used. Suitable base material molecules are any substance which can approach and interact with the surface by adsorption or other chemical process, and have accessible functional groups to which additional substances, as for example, binding agents can be attached. As an example, the reference has used a derivative of a polyethylene glycol. The properties of this molecule allow for its use as a base material molecule. Each molecule of this polymer has four amine groups, which can serve as linkage sites for the conjugation of additional substances. The hydrophobic backbone of the polyethylene derivative interacts with the particle and is attached to the particle surface by adsorption or some other process. This interaction is very strong. The amine groups do not appear to interact with the particle surface and are accessible as conjugation sites for the attachment of additional substance, such as, binding agents. Using this polymer as the base molecule they have prepared two different types of particle-binding agent reagents. One reagent contains biotin groups as binding agents and the other particle-binding agent reagent was made to contain single-stranded nucleic acids as binding

agents. The biotin used for attachment was a chemically modified form where it will covalently link to amine groups. For the nucleic acids, the 5' ends were chemically modified so that they would chemically react with the amine groups. Linker arms of various lengths and composition can also be incorporated into the molecular structure. For example, a small molecular weight base material molecule an be used where it's molecular structure is optimized for attachment to the particle or surface, attachment of most any substance to it with any desired orientation, and with a high level of binding activity. As an example, a linear polypeptide twenty amino acids in length is chemically modified at one terminus by the addition of disulfide or thiol chemical groups. The native polypeptide is composed of amino acids such that the polypeptide chain will not interact with the surface except through the chemically modified end. At the other terminus a free amino group exists, or alternatively, has been chemically modified for a desired conjugation process such that most any substance can be attached at this position. This low molecular weight base material molecule then is used in one or more variations of the methods as described herein. (col. 77-81). The polyethylene glycol or the polypeptide is viewed to be inclusive of the spacer portion of instant claim 243 for example. And the amine group is viewed to be inclusive of the functional group.

10. Claims 433-436, 439-442, 444-446 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Coffer et al. (Nanotechnology (1992) 3: 69-76).

Coffer teaches the attachment of an oligonucleotide to a semiconductor nanoparticle at a surface density sufficient so that the nanoparticles are stable (see pages 69-72 and 75).

11. Claims 433-437, 439-446 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over by Chavany et al. (Pharmaceutical Research (1994) 11(9): 1370-1378).

Chavany teaches the attachment of an oligonucleotide to a nanoparticle at a surface density sufficient so that the nanoparticles are stable (see pages 1370-1372, 1375 and 1377).

12. As it is pointed in *In re Fitzgerald* (205 USPQ), page 594, 2nd col. , 1st full paragraph supports the shifting of the burden of proof to the applicant that the instantly claimed invention is novel and unobvious over the prior arts. Since both the prior art and the instant application prepare and use composition which appeared to be identical.

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is noted that, the recitation of surface density will be obvious, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least one" of

the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad and encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to nanoparticles.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Thursday, April 22, 2004

JEZIA RILEY
PRIMARY EXAMINER